**A Primer: Two NT-related Diseases with Increasing Incidence among the Elderly – AD and PD**

*Describe epidemiology, behavioral manifestations, and major pathological characteristics of Alzheimer’s and Parkinson’s Diseases*

**AD**

* Acceleration of AD prevalence at 70 years and older
* Behaviors common in AD
  + Memory deficits, especially in recent memory
  + Cognitive decline
  + Progressive degeneration
  + Age-related expression beginning at 4th decade of life
* Neuropathology
  + Senile plaques
    - Primarily composed of beta-amyloid protein (made from abnormal cleavage fragments)
      * It is very dense and a sticky extracellular deposit
    - Process leading to this is unknown
  + Neurofibrillary tangles
    - Paired helical filaments within the cytoplasm primarily composed of a hyperphosphorylated form of tau (normal molecule of neuronal MTs)
    - Process leading to this is unknown
  + Cholinergic deficit in nucleus basalis
    - Leads to memory loss, especially in recent memory
  + Generalized neuronal loss as the disease progresses
    - This leads to loss of most memory and no recognition of close family members or caregivers who work with them daily
    - Highly prominent on a MRI

**PD**

* Similar to AD in that neuronal loss is present, but dissimilar in that it is a specific type of neuron and its projections
* Common Symptoms
  + Constant tremor at rest
  + Muscle and limb rigidity
  + Limited initiation of movement ->lacking facial expression
  + Diminished spontaneous movements
  + Characteristic Signs
    - Shuffling gait and postural rigidity
    - Slow speech
    - Difficulty in manipulating objects
* Neuropathology
  + Loss of dopaminergic neurons leads to reduced activation from basal ganglia to thalamus to motor ctx
    - Results in the motor problems and other observations

*Consider evidence for the causes of Alzheimer’s and Parkinson’s diseases*

**AD**

* Might be multifactorial, but the following have supporting evidence
* Infectious Agent
  + Viral-like agents form aggregates in the brain
* Toxin
  + Aluminum or other environmental toxins might contribute to sporadic AD via oxidative stress
* Abnormal Protein
  + Abnormal proteins compose plaques and tangles
  + NFTs are a result of hyper-phosphorylation of the MT-associated protein, tau
    - This disrupts MT stability and results in cell death as cell’s machinery gets clogged
  + Plaque form from abnormal cleavage of APP that is coded by protein beta-amyloid
* Genetic
  + There is increased deposition of Aβ in the 42 AA form, leading to greater aggregation and formation of senile plaques
  + Evidence for multi-focal genetic component
    - Down syndrome is intimately associated with AD
    - Late onset AD is correlated with presence of E4 allele on Chrom 19
    - In 25% of cases, familial inheritance is observed
      * Found on Chr 21, 14, 1
      * Mutations in the presenilin proteins promote formation of Aβ and FAD
* Acetylcholine
  + Cholinergic Approach
    - Cholinergic neurons of the nucleus basalis degenerate in AD
    - Since these neurons are widespread in cortex and hippocampus, destruction of these connections manifest themselves as recent memory loss
  + Glutamatergic Approach
    - As neurons die, they release significant glutamate in the cortex damaging nearby neurons causing a cascading event

*Reflect on key differences between these two conditions as well as issues of disease progression, limitations of current therapy in efficacy and potential for adverse events, and new therapies or means of early detection.*

**AD**

* Aricept
  + Passes the blood-brain barrier and reversibly blocks AChE
  + It doesn’t alter disease progression, but allows for greater functioning at earlier stages
  + Only effective in these earlier stages
* Nemenda
  + Partial NMDA antagonist that attempts to rescue surviving neurons
  + Not useful for mild and moderate AD because antagonizing NMDA would be counterproductive to memory formation

**PD**

* L-Dopa
  + Velocity and acceleration of voluntary movement are substantially improved with L-Dopa
* Pallidotomy
  + Lesioning of GBi to reduce negative influence on the thalamus to increase motor fxn
* Chronic or controlled electrical pulse stimulation of ventral anterior or ventral lateral thalamus
  + Avoids lesioning problem, while also stimulating thalamus to output more onto motor ctx